SUPPLEMENTARY MATERIALS

Supplementary Methods

Inclusion criteria

Patients enrolled in this study had to meet the following criteria:

1. Confirmed asthma diagnosis
2. Use of high-dose inhaled corticosteroid (ICS)[a] and 2nd controller[b] ≥3 months before registration
3. Uncontrolled asthma meeting ≥1 of the following criteria:

   a) Poor symptom control: Asthma Control Questionnaire (ACQ)-5 score ≥1.5 or Asthma Control Test score <20[c]

   b) Frequent exacerbations: at least 2 asthma exacerbations in the 12 months before enrollment

   c) Airflow obstruction: predicted pre-bronchodilator forced expiratory volume in 1 second (FEV_1) <80% (FEV_1/forced vital capacity less than the lower limit of normal)[c,d]
4. Investigator judged the need to strengthen the treatment with biologics for patient's asthma treatment and the patient received an explanation from the investigator
5. Patient deemed capable of visiting their study site regularly during the next 24 months
6. Patient provided written informed consent to participate in this study
7. Aged ≥20 years at the time of providing informed consent.

[a]High-dose ICS per day (Japanese guidelines for adult asthma 2018)

[b]Plus 2nd controller: any of the following: long-acting β_2-adrenoceptor agonist, long-acting muscarinic antagonist, leukotriene receptor antagonist, sustained-release theophylline, oral corticosteroid

[c]ACQ-5 and/or Asthma Control Test, or FEV_1 at registration or within 4 weeks before registration could be used for poor symptom control or airflow obstruction

[d]Acceptable post-bronchodilator FEV_1

Exclusion criteria

Patients who met any of the following criteria were excluded:

1. Participated in other interventional studies such as clinical trials, within the last 8 weeks
2. Were using biologics at registration
3. Diagnosed with chronic obstructive pulmonary disease
4. Planned to receive bronchial thermoplasty therapy in the near future
5. Receipt of any marketed or investigational biologics within 5 months prior to enrollment
6. Presence of any disorder, including but not limited to: cardiovascular, gastrointestinal, hepatic, renal, neurological, musculoskeletal, infectious, endocrine, metabolic, hematological, psychiatric, or major physical impairment in an acute phase that in the opinion of the investigator could:
    - Affect the safety of the patient throughout the study
    - Influence the findings of the study or its interpretation
    - Impede the patient's ability to complete the entire duration of study.

List of participating study sites

- Kindai University Hospital
- Osaka Metropolitan University Hospital
- St. Marianna University Yokohama Seibu Hospital
- Tokyo Women's Medical University Hospital
- Toho University Ohashi Medical Center
- Kobe University Hospital
- Sagamihara National Hospital
- Yokohama City Minato Red Cross Hospital
- Niigata University Medical & Dental Hospital
- Yokohama City University Hospital
- Yokohama City University Medical Center
- Okayama Rosai Hospital
- Showa University Hospital
- Osaka City General Hospital
- Okayama University Hospital
- Teikyo University Hospital
- Tottori University Hospital
- Fujita Health University Bantane Hospital
- Kochi Medical School Hospital
- National Hospital Organization Minami-Okayama Medical Center
- Okayama City Hospital
- Shiga University of Medical Science Hospital

- Kindai University Nara Hospital
- Saitama Prefectural Cardiovascular and Respiratory Center
- Kyushu Central Hospital of the Mutual Aid Association of Public School Teachers
- Nagoya City University Hospital
- Asahikawa Medical University Hospital
- Gunma University Hospital
- Yamagata University Hospital
- Shizuoka General Hospital
- Hamamatsu University Hospital
- Juntendo University Hospital
- Hiroshima Allergy & Respiratory Clinic
- Mazda Hospital